EXPERIMENTAL DATA

Ca-Fructoborate: D-Fructose (2.16 g) is dissolved in water (4 ml) at room temperature. Boric acid (0.372 g) is then added to the thus prepared solution, and upon its dissolving calcium carbonate (0.246 g) is added in small portions. After carbon dioxide evolution has ceased, acetone (99%, p.a. quality; 20 ml) is added to the reaction mixture, whereupon a colorless oil separates at the bottom of the reaction vessel. Two layers are separated using a separating funnel, and the lower layer (crude boron complex) is treated again with acetone. Upon standing at room temperature for one hour, the mixture is triturated using a glass rod to induce crystallization, and the oil slowly solidifies. This produces a white crystalline solid. The solid is filtered off on a Buchner funnel, washed with additional acetone, and air dried. The solid is then further dried in a vacuum oven at room temperature, leaving a solvent free, very pure Ca-fructoborate. The yield is typically 2.05 g (75%).

Pharmacokinetic Studies: Test Animals: Adult male Sprague Dawley rats (n=24 enrolled, n=6 per group); Animal Feed: AIN76 Low Borron Rodent Chow, Diet No. 116314, Lot No. 8182-7 (Dyets, Inc.). Time Points: Plasma: 0, 0.5, 1, 2, 6, 12, 24, and 48 hours; Urine: -12 to 0, 0 to 6, 6 to 12, 12 to 24, and 24 to 48 hours; Fecal: -12 to 0, 0 to 12, 12 to 24, and 24 to 48 hours. Analytical Methods: Boron concentration of plasma and urine samples were analyzed by Inductively Coupled Plasma-Mass Spectrometry. Pharmacokinetic parameters determined: Cmax, Tmax, AUCT, AUC, CL/F (Groups 2 and 4 only), Vz/F (Groups 2 and 4 only), Ae48, fe48, Cmax/Dose, and AUC/Dose. Analysis was accomplished using validated Excel spread sheet analysis. Pharmacokinetic Results: The pharmacokinetic characteristics of boron were determined in rats following oral gavage administration of 43 and 1000 mcg/kg elemental boron as calcium fructoborate and boron citrate. Statistical Methods: Parametric ANOVA was used to compared pharmacokinetic parameters within dose groups (i.e., Group 1 versus Group 3, and Group 2 versus Group 4). ANOVA was accomplished using SAS (version 6.12) to analyze the following pharmacokinetic endpoints: Cmax, Tmax, AUCT, AUC,

CL/F, Vz/F, Az, tom,Ae48, fe48, Cmax/Dose, and AUC/Dose. A p-value of 0.05 or less was considered to be statistically significant.

Animals: Twenty-four normal healthy adult male Sprague Dawley rats (Harlan Sprague Dawley Inc., San Diego, CA) weighing between 250 - 350 g were used in this study. The rats were selected for the study based on a visual appraisal of good physical condition and conformance to body weight specifications. Each rat had a numbered ear tag to identify the animal. In addition, each rat's cage was identified by a cage card listing the animal identification number, study number, group assignment and sex of the animal. Rats were housed in standard wire caging during the acclimation period and in stainless steel or plastic metabolic cages during the treatment periods.

Rats were observed on a daily basis during acclimation and treatment time periods. Equal numbers of animals from each group were assigned to either plastic or stainless steel metabolic caging. In addition, environmental monitoring of temperature, humidity, and light was conducted, and animal housing area and equipment were cleaned and/of sanitized.

Treatment Assignments: This was a randomized, single-dose, open-labeled, bioequivalence study consisting of a total of twenty-four rats. The study consisted of four groups. Each rat was randomly assigned to a group at the start of the study. A summary of the study design is presented in Table 1.

Treatment Administration: A single dose was administered to the rat by oral gavage using a gavage needle pre-filled with the assigned test article solution. The following doses were administered: Group 1: 43 mcg/kg elemental boron from 1.6 mg/kg calcium fructoborate; Group 2: 1000 mcg/kg elemental boron from 37.5 mg/kg calcium fructoborate; Group 3: 43 mcg/kg elemental boron from 860 mcg/kg boron citrate; Group 4: 1000 mcg/kg elemental boron from 20 mcg/kg boron citrate; Feed: The rats were fasted overnight prior to administration of test articles and 4 hours after administration. At all other times, the rats had *ad libitum* access to AIN76 Low Boron Rodent Chow, Diet No. 116314 (Dyets, Inc., Lot No. 8182-7). Rats were started on the AIN76 Low Boron Rodent Chow for 14 days prior to treatment. A sample of the feed was sent to

WCAS for analysis of boron content. The boron content by ICP-MS for the feed was found to be 0.2 to 0.3 ppm.

Time Points: Blood specimens for the determination of boron in plasma were collected from the tail vein of each rat at 0 (pre-dose), 0.5, 1, 2, 6, 12, 24 and 48 hours post-dose. These time points were selected based on a review of the scientific literature. The estimated elimination tin of boron in rats is approximately 12 hours. The accumulated urine and fecal specimens were collected at the following time points: 0 (pre-dose) Time Point: The accumulated urine and fecal specimens were collected approximately 12 hours before dosing to immediately before dosing. 6-hour Post-dosing Time Point The accumulated urine and fecal specimens were collected just after oral dosing to 6-hours post-dosing. 12-hour Post-dosing Time Point: The accumulated urine and fecal specimens were collected between 6-hour post-dosing to 12 hours post-dosing. 24-hour Post-dosing Time Point: The 24-hour post-dosing accumulated urine and fecal specimens were collected between 12-hour post-dosing to 24 hours post-dosing. 48-hour Post-dosing Time Point: The 48-hour post-dosing accumulated urine and fecal specimens were collected between 24-hour post-dosing to 48-hour post-dosing.

Observations and Measurements: A physical examination of each rat was conducted prior to initiation of treatment. Only animals that were considered normal and in good health were allowed to be included in the study. The rats were weighed on a calibrated scale on Day -1 and only those rats that weighed between 250 g and 350 g were allowed to be included in the study.

Specimens: Approximately 0.5 mL of whole blood was collected from the tail vein of each rat into a polypropylene tube containing lithium heparin at the time points indicated in Section 3.7. The plasma was separated within 30 minutes of collection by centrifuging at 1200 x G at 2 to 8°C for 10 minutes. The plasma was then aspirated, transferred to a fresh polypropylene vial for freezing, snap frozen in liquid nitrogen and stored at -80 to -60°C. Urine and fecal specimens were collected from the metabolic cages of each rat at the time points indicated above in Section 3.7. The specimens were frozen after collection and stored at -80 to -60°C.

Analytical Methods: The boron concentrations in each sample (plasma or urine specimens or boron citrate, calcium fructoborate, water or feed samples) were determined by Inductively Coupled Plasma-Mass Spectrometer (ICP-MS) at WCAS (WCAS SOP 7090 Rev 1). In ICP-MS, positive ions generated by the plasma are introduced into a vacuum interface. Following the interface is a quadrapole mass spectrometer. During sample introduction, the mass spectrometer scans a range of masses. Data is collected in a multi-channel analyzer. The response for each mass is used to calculate the concentration for an element in solution by comparison with standards. Prior to analysis by ICP-MS, the samples provided from the rat study and reference samples supplied by were prepared for sample introduction.Urine samples were treated as follows: 200 mcl of an internal standard (boron-10) and 1 mL of nitric acid were added to 200 mcl of the urine sample and diluted to 20 g with deionized water in an autosampler tube (1 mL=1 g). Plasma samples were treated as follows: 20 mcl, of an internal standard (boron-10) was added to 50 mcl of the plasma sample and diluted to 2 g with 0.1% ammonium hydroxide solution in an autosampler tube (1 mL=1 g). Calcium fructoborate and boron citrate samples were treated as follows: 0.2 g of sample was dissolved in 30 mL of deionized water. To this solution was added 5 mL of nitric acid and 1000 mcl of boron-10 internal standard. The solution was diluted with deionized water to 100 g (1 mL=1 g). The internal standard is a boron-10 isotopically enriched boric acid NIST standard. Once the samples were ready for analysis and the instrument was calibrated against two calibration blanks, calibration standards (200, 100, 50, 10, 5, 1 mcg/l), and reagents blanks, the samples were analyzed. A continuing calibration standard was analyzed after every 10 or fewer samples.

Pharmacokinetic Parameters: Pharmacokinetic parameters determined included the following: the maximum plasma concentration (Cmax), the time of the maximum plasma concentration (Tmax), the area under the plasma concentration versus time curve from time 0 to the time (t) of the last observed plasma concentration (AUCT), the area under the curve from time 0 to time infinity (AUC), the apparent terminal phase disposition rate constant (Az), the apparent terminal phase elimination half-life ($t_{,,,}$), the oral total body clearance (CL/F), the apparent volume of distribution following extravascular adminictration (Vz/F), the total amount of boron excreted in the urine from

time 0 to 48 hours (Ae48), and the fraction of the dose excreted in the urine from 0 to 48 hours (fe48). In addition, Cmax/Dose and AUC/Dose were determined.

Pharmacokinetic Analysis: Noncompartmental pharmacokinetic analysis of each individual data set (all plasma boron concentration data and the amount of boron excreted from time 0 to 48 hours) using validated Excel (version 5.0/Windows 95) spread sheet analysis. Spread sheet validation was accomplished using WinNonlin Professional (version 1.5). Cmax and Tmax values were taken directly from the observed data. λz estimates were estimated from all plasma concentration-time values on the log-linear terminal elimination phase (not less than the last three observed concentrations). Half-life values were determined as $t1/2 = 0.693/\lambda z$. AUCT was estimated by linear trapezoidal rule from time 0 to time t, where t is the time of the last observed plasma concentration. AUC was estimated as AUC = AUCT $Ct/\lambda z$, where C, is the last observed plasma concentration at time t. Cmax/Dose and AUC/Dose were determined by normalizing the respective values to a 1 mg/kg elemental boron dose. The amount of boron excreted in each urine collection interval was determined as Amount (interval) = Urinary Concentration (interval) * Urine Volume (interval). The total amount of boron excreted was calculated as the sum of all individual collection period amounts. The Ae48 was corrected for the amount of boron excreted during a comparable baseline period as Ae48 = (Ae (0 to 48 hr)-[Ae (-12 to 0 hr)]*4}. The fraction excreted in the urine from 0 to 48 hours expressed as a percent was determined as fe48 = [Ae48/Dose]*100. CL/F was determined as CL/F = Dose/AUC, and Vz/F was determined as $Vz/F = Dose/\lambda z*AUC$.

Statistical Analysis: Parametric (normal-theory) general linear model (GLM) analysis of variance (ANOVA) techniques were used to compare pharmacokinetic parameters within dose groups (i.e., Group 1 versus Group 3, and Group 2 versus Group 4). ANOVA was accomplished using SAS (version 6.12) to analyze the following pharmacokinetic endpoints: Cmax, Tmax, AUCT, AUC, CL/F, Vz/F, Az, Ae48, fe48, Cmax/Dose, and AUC/Dose. A p-value of 0.05 or less was considered to be statistically significant for the comparisons. All boron concentrations the below quantification limit (BQL, 0.02 mcg/mL boron for plasma and 0.05 mcg/mL boron for urine) were treated as zero for the analyses and presentation. All pharmacokinetic and statistical analyses were

performed on non-rounded data and parameter estimates. All parameters were rounded to 3 or 4 significant figures for presentation. Plasma concentration versus time data, urine data, and pharmacokinetic parameter data were summarized and presented by treatment and/or dose group using the following descriptive statistics: n, mean, SD, CV%, SEM, minimum, median, and maximum.

Pharmacokinetic Profile: Following administration of 43 mcg/kg elemental boron as calcium fructoborate (Group 1) or boron citrate (Reference Compound, Group 3), mean Cmax plasma boron concentration values of 0.038 and 0.044 mcg/mL were observed at mean Tmax values of 1.2 and 1.9 hours in Groups 1 and 3, respectively. Mean AUCT values of 0.060 and 0.118 mcg/mL*hr were observed in Groups 1 and 3, respectively. Insufficient post-absorption data were available to permit determination of λz or t1/2. Accordingly, determination of AUC, CL/F, and Vz/F were not possible. Mean Ae48 values for Groups 1 and 3 were 12.5 and 11.7 mcg, respectively, corresponding to mean fe48 values of 89.5% and 81.9%, respectively.

Following administration of 1000 µg/kg elemental boron as calcium fructoborate (Group 2) or boron citrate (Reference Compound, Group 4), mean Cmax plasma boron concentration values of 0.77 and 0.54 mcg/mL were observed at mean Tmax values of 0.9 and 0.9 hours in Groups 2 and 4, respectively (Table 5). Mean AUCT values of 4.74 and 3.07 mcg/mL*hr and mean AUC values of 4.99 and 3.38 mcg/mL*hr were observed in Groups 2 and 4, respectively. Mean CL/F values were 204 and 301 mL/hr/kg for Groups 2 and 4, respectively, and mean Vz/F values were 1.46 and 1.75 L/kg, respectively. Mean t1/2 values of 5.0 and 4.1 hours were observed for Groups 2 and 4, respectively. Mean Ae48 values for Groups 2 and 4 were 197.1 and 138.1 mcg, respectively, corresponding to mean fe48 values of 62.8% and 45.4%, respectively. If the mean fe48 values were considered to be accurate estimates of the absolute extent of availability of boron, then the mean total body clearance (CL) values would be approximately 128 and 137 mL/hr/kg for Groups 2 and 4, respectively, and mean apparent volume of distribution (Vz) values would be approximately 0.92 and 0.78 L/kg, respectively.

LC-MS detection of Ca-Fructoborate in Serum: Using LC-MS, Ca-Fructoborate was detected and measured from serum samples at concentrations as low as 0.2 ppm and higher as presented in **Figure 1**. This method was used to analyze the presence and amount of Ca-Fructoborate in serum collected from mice treated orally (guavage) with Ca-Fructoborate in liquid at dose 600 mcg/mouse for 30 and 60 minutes. Results show clearly that Ca-Fructoborate was delivered from intestine to bloodstream in intact form and in time-dependent manner, which is reflected in the Table below. The here obtained data show for the first time that Ca-fructoborate can serve as a controlled-release source of boron in blood and tissues and is not likely to be a pre-from of boric acid. Based upon the amount of Ca-fructoborate provided per mouse (20g by average) the collected results show that bioavailability of the compound is as high as 556 mcg/ml of serum.

Sample	Time of Treatment	Intact Ca-fructoborate [mcg/mL]
Untreated	0	*below detection
1.	30 minutes	449
2.	60 minutes	556

*Detection limit – 3 mcg/mL

Detection of intact Ca-Fructoborate in sera collected from fasted mice treated orally with the compound for 30 or 60 minutes. Collected sera were diluted in running buffer and filtered through 0.45 PVDF filter. This solution was analyzed by LCMS for Ca-Fructoborate as the fructoborate anion.

Results and Discussion: The plasma boron concentrations observed following oral gavage administration of 43 mcg/kg elemental boron as calcium fructoborate (Group 1) or boron citrate (Reference Compound, Group 3) were uniformly low reflecting the similarity of this dose level with the normal level of dietary boron intake. The range of maximum plasma boron concentrations observed (0.030 to 0.053 mcg/mL) were consistent with those anticipated following ingestion of normal dietary amount of elemental boron. Measurable plasma boron concentrations generally were not observed

past the 2-hour sample collection with the exception of two animals in Group 3, in which measurable concentrations persisted to the 6-hour sample collection. Accordingly, comparison of the AUCT values as an assessment of the relative extent of systemic availability of boron from the two 43 mcg/kg elemental boron formulations was not appropriate.

Urinary excretion of boron following both oral gavage administration of 43 mcg/kg elemental boron as calcium fructoborate (Group 1) or boron citrate (Reference Compound, Group 3) were uniformly high, again reflecting the similarity of this dose level with the normal level of dietary boron intake. The mean fraction of dose excreted in 48 hours in both 43 mcg/kg elemental boron treatment groups were consistent with those observed in other studies utilizing comparable oral doses. The relative extent of availability of boron from the two formulations based upon Ae48 was 1.068 (i.e., 12.5 mcg/11.7 mcg), or 106.8%, for the comparison of calcium fructoborate (Group 1) to boron citrate (Reference Compound, Group 3). No significant differences were observed in Ae48 between the two 43 mcg/kg elemental boron treatment groups ($p=0.797$), indicating that the relative extent of availability of calcium fructoborate based upon urinary excretion data was similar to boron citrate (Reference Compound) at this low dietary level of oral intake.

The plasma boron concentrations observed following oral gavage administration of 1000 mcg/kg elemental boron as calcium fructoborate (Group 2) or boron citrate (Reference Compound, Group 4) were approximately 15- to 25-fold higher than those observed following oral gavage administration of 43 mcg/kg elemental boron as anticipated reflecting the pharmacologic dose of boron. Following the apparent first-order absorption phase, plasma boron concentrations appeared to decline in a log-linear, mono-exponential manner, indicating that boron exhibited probable first-order elimination characteristics at this dose level. Measurable plasma boron concentrations generally were observed out to the 24-hour sample collection.

The mean maximum plasma boron concentration observed for calcium fructoborate group (Group 2) was approximately 20-fold higher than the mean Cmax

observed in low dose calcium fructoborate group (Group 1). The mean maximum plasma boron concentration observed for boron citrate group (Reference Compound, Group 4) was approximately 12-fold higher than the mean Cmax observed in low dose boron citrate group (Group 3). These data indicated that calcium fructoborate exhibited a nearly linear increase in Cmax with the approximate 23-fold increase in elemental boron dose. The mean Cmax/Dose values from both of the high dose groups were consistent with the mean Cmax/Dose values from the two low dose groups, indicating that boron appeared to exhibit linear pharmacokinetic characteristics over the dose range studied following administration of both formulations.

Mean CL/F values were consistent between the two high dose groups (Groups 2 and 4) and varied only approximately 1.4-fold. When corrected for the approximate absolute extent of availability based upon the urinary excretion data and transformed to mL/min/70 kg estimates, the observed CL values ranged from approximately 149 to 155 mL/min/70 kg. These values were consistent with the reported elimination of boron by the kidneys as previously reported. This range of clearance values indicated probable clearance of boron by a combination of glomerular filtration and active tubular secretion. Mean Vz/F values from the two groups (Groups 2 and 4) were also consistent and varied only approximately 1.2-fold. When corrected for the approximate absolute extent of availability based upon the urinary excretion data the mean Vz estimates were comparable to total body water. These findings are consistent with the reported distribution of boron throughout body water.

The resulting mean t1/2 values (approximately 4.1 to 5.0 hours) were similar for the two groups and somewhat shorter than the 12 hour half-life reported in other studies. Examination of the individual plasma concentration versus time profiles provided evidence that the half-life of boron may have been under estimated in some animals from both 1000 mcg/kg elemental boron treatment groups. This occurred when the last two measurable concentrations reflected an apparent terminal elimination phase that was not well described by the last three measurable plasma concentrations upon which the individual half-life was estimated. Accordingly, the actual half-life of boron in the 1000

mcg/kg elemental boron treatment groups was probably longer than the mean half-life estimates observed.

The plasma boron concentrations following administration of 1000 mcg/kg elemental boron as calcium fructoborate (Group 2) were consistently higher than those observed following administration of 1000 mcg/kg elemental boron as boron citrate (Reference Compound, Group 4). Accordingly, the mean AUCT values were approximately 1.5-fold for calcium fructoborate group, and the mean AUC values were approximately 1.4-fold higher for the calcium fructoborate group. Assessment of the relative extent of systemic availability of boron from the two formulations based upon comparison of the mean AUC resulted in a Frel for calcium fructoborate of 1.476 (i.e., 4.985 mcg/mL*hr/3.377 mcg/mL*hr), or approximately 147%. The difference in mean Cmax and mean AUC values between these two 1000 mcg/kg elemental boron treatment groups were statistically significant (p 0.002 and p 0.003, respectively). These data indicated that the relative extent of availability of calcium fructoborate based upon plasma boron concentration data was superior to boron citrate (Reference Compound) at this high dose level.

The urinary excretion of boron following oral gavage administration of 1000 mcg/kg elemental boron both as calcium fructoborate (Group 2) or boron citrate (Reference Compound, Group 4) was variable. The mean fe48 values were lower than the approximately 90% value reported in the literature. The mean Ae48 and fe48 values were higher following administration of calcium fructoborate than following administration of boron citrate. The relative extent of availability of boron from the two formulations based upon Ae48 was 1.427 (i.e., 197.1 mcg/13 8.1 mcg) or approximately 143% for the comparison of calcium fructoborate (ProBoronTM, Group 2) to boron citrate (Reference Compound, Group 4). Although the difference in mean Ae48 between the two 1000 mcg/kg elemental boron treatment groups were not significantly different, the relative extent of availability of boron based upon urinary excretion data was in excellent agreement with the relative extent of availability estimates based upon plasma boron concentration data and indicated that the systemic availability of calcium fructoborate was superior to boron citrate (Reference Compound) at this high dose level.

In further contemplated experiments, complexes with association constants of less than 2,000 are considered to fail to protect boron from being released from the complex. Therefore, such complexes with relatively low association constants will typically exhibit non-specific boron delivery and most typically fail to improve bone ash and bone density. Similarly, complexes with relatively high association constant (e.g., 16,000) will fail to release the boron from the complex and will therefore be unavailable to remedy boron deficiency associated conditions.

Conclusions: The disposition and pharmacokinetics of boron in plasma and urine were determined following single-dose oral gavage administration of 43 and 1000 mcg/kg elemental boron as calcium fructoborate or boron citrate (Reference Compound) to rats (n=22). Boron disposition at both dose levels, and for both compounds, appeared to be consistent with first-order absorption, distribution throughout total body water, and first-order elimination by renal mechanisms. Based upon the comparison of maximum plasma concentrations, boron appeared to exhibit linear pharmacokinetic characteristics over the dose range studied.

The relative extent of systemic availability of boron based upon the amount of boron excreted during the first 48 hours following administration 43 mcg/kg elemental boron as calcium fructoborate was approximately 107% when compared to boron citrate (Reference Compound). No significant difference was observed between the mean Ae48 values from these two 43 mcg/kg elemental boron treatment groups indicating that the relative extent of availability from calcium fructoborate was similar to boron citrate (Reference Compound) based upon urinary excretion data at this low dietary level of intake.

The relative systemic availability of boron based upon the area under the plasma boron concentration versus time curve following administration 1000 mcg/kg elemental boron as calcium fructoborate was approximately 147% when compared to boron citrate (Reference Compound). The difference in mean Cmax and mean AUC values between these two 1000 mcg/kg elemental boron treatment groups were statistically significant ($p=0.002$ and $p=0.003$, respectively) indicating that the relative extent of availability of

boron from calcium fructoborate was superior to the systemic availability of boron from boron citrate (Reference Compound) based upon plasma boron concentration data at this high dose level.

The relative extent of systemic availability of boron based upon the amount of boron excreted during the first 48 hours following administration 1000 mcg/kg elemental boron as calcium fructoborate was approximately 143% when compared to boron citrate (Reference Compound). Although the difference in mean Ae48 between the two 1000 mcg/kg elemental boron treatment groups were not significantly different, the relative extent of availability of boron based upon urinary excretion data was in excellent agreement with the relative extent of availability estimates based upon plasma boron concentration data and indicated that the systemic availability of boron from calcium fructoborate was superior to the systemic availability of boron from boron citrate (Reference Compound) at this high dose level.

The pharmacokinetics of boron were determined following single-dose oral gavage administration of 43 and 1000 mcg/kg elemental boron as calcium fructoborate or boron citrate (Reference Compound) to rats (n=22). Boron disposition at both dose levels and for both compounds appeared to be consistent with first-order absorption, distribution throughout total body water, and first-order elimination primarily by renal mechanisms. Mean CL estimates (Groups 2 and 4) exceeded glomerular filtration and indicated probable clearance by a combination of glomerular filtration and active tubular secretion. Mean Vz estimates (Groups 2 and 4) approximated total body water indicating that boron appeared to distribute throughout total body water. Boron appeared to exhibit linear pharmacokinetic characteristics over the dose range studied.

The relative extent of systemic availability of boron based upon the amount of boron excreted during the first 48 hours following single-dose oral gavage administration 43 mcg/kg elemental boron as calcium fructoborate was approximately 107% when compared to an equivalent dose of boron citrate (Reference Compound). No significant differences were observed in Ae48 ($p=0.797$) indicating that the two formulations

exhibited similar relative extent of systemic availability of boron based upon the amount of boron excreted during the first 48 hours at this low dose level.

The relative systemic availability of boron based upon the area under the plasma boron concentration versus time curve following single-dose oral gavage administration 1000 mcg/kg elemental boron as calcium fructoborate was approximately 147% when compared to an equivalent dose of boron citrate (Reference Compound). The relative extent of systemic availability of boron based upon the amount of boron excreted during the first 48 hours following administration 1000 mcg/kg elemental boron as calcium fructoborate was approximately 143% when compared to an equivalent dose of boron citrate (Reference Compound). Significant differences were observed in Cmax ($p=1002$) and AUC ($p=0.003$) indicating that calcium fructoborate exhibited superior relative extent of systemic availability of boron when compared to boron citrate (Reference Compound) based upon plasma boron concentration versus time data at this high dose level.